

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference 8940.0033-304	FOR FURTHER ACTION	See item 4 below
International application No. PCT/US2005/001883	International filing date (<i>day/month/year</i>) 21 January 2005 (21.01.2005)	Priority date (<i>day/month/year</i>) 21 January 2004 (21.01.2004)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant FIVE PRIME THERAPEUTICS, INC.		

1.	This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).																								
2.	<p>This REPORT consists of a total of 9 sheets, including this cover sheet.</p> <p>In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.</p>																								
3.	<p>This report contains indications relating to the following items:</p> <table style="width: 100%; border: none;"> <tr> <td style="width: 15%;"><input checked="" type="checkbox"/></td> <td style="width: 35%;">Box No. I</td> <td style="width: 50%;">Basis of the report</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table>	<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input checked="" type="checkbox"/>	Box No. II	Priority	<input checked="" type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input checked="" type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input type="checkbox"/>	Box No. VIII	Certain observations on the international application
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4.	The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).																								

<p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No. +41 22 338 82 70</p>	<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 50%;">Date of issuance of this report 18 October 2006 (18.10.2006)</td> <td style="width: 50%;">Authorized officer</td> </tr> <tr> <td colspan="2" style="text-align: center; padding: 10px;"> <p style="font-size: 1.2em;">Simin Baharlou</p> </td> </tr> <tr> <td colspan="2">e-mail: pt09@wipo.int</td> </tr> </table>	Date of issuance of this report 18 October 2006 (18.10.2006)	Authorized officer	<p style="font-size: 1.2em;">Simin Baharlou</p>		e-mail: pt09@wipo.int	
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e-mail: pt09@wipo.int							

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)

To:

see form PCT/ISA/220

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/US2005/001883

International filing date (day/month/year)
21.01.2005

Priority date (day/month/year)
21.01.2004

International Patent Classification (IPC) or both national classification and IPC
INV. C07K16/18 A61P37/02

Applicant
FIVE PRIME THERAPEUTICS, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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D-80298 Munich
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Date of completion of
this opinion

see form
PCT/ISA/210

Authorized Officer

Rankin, Robert

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2005/001883

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:
 - ☒ the international application in the language in which it was filed
 - ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ on paper
 - ☐ in electronic form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in electronic form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

Box No. II Priority

1. ☒ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43*bis*.1 and 64.1) is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of

- ☐ the entire international application
- ☒ claims Nos. 11, 23, 26, 29, 32, 35, 38, 41, 44, 47, 52-77 (completely) 12-22, 24, 25, 27, 28, 30, 31, 33, 34, 36, 37, 39, 40, 42, 43, 45, 46, 50, 51 (incompletely)

because:

- ☒ the said international application, or the said claims Nos. 13-22, 24, 25, 27, 28, 30, 31, 33, 34, 36, 37, 39, 40, 42, 43, 45, 46, 48, 50, 51 (partially, for reasons of industrial applicability) relate to the following subject matter which does not require an international search (*specify*):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):
- ☒ no international search report has been established for the whole application or for said claims Nos. 11, 23, 26, 29, 32, 35, 38, 41, 44, 47, 52-77 (completely) 12-22, 24, 25, 27, 28, 30, 31, 33, 34, 36, 37, 39, 40, 42, 43, 45, 46, 50, 51 (incompletely)
- ☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:
- ☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
- ☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
- ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13ter.1(a) or (b).
- ☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- ☐ See Supplemental Box for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2005/001883

Box No. IV Lack of unity of invention

1. ☐ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has, within the applicable time limit:
- ☐ paid additional fees
 - ☐ paid additional fees under protest and, where applicable, the protest fee
 - ☐ paid additional fees under protest but the applicable protest fee was not paid
 - ☐ not paid additional fees
2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
 - ☒ not complied with for the following reasons:
see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☒ all parts.
 - ☐ the parts relating to claims Nos.

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	15-17, 19-21, 24, 25, 27, 30, 33, 34, 26, 39, 40, 42, 45
	No: Claims	1-10, 12-14, 18, 22, 50, 51
Inventive step (IS)	Yes: Claims	
	No: Claims	1-10, 12-22, 24, 25, 27, 30, 33, 34, 36, 39, 40, 42, 45, 50, 51
Industrial applicability (IA)	Yes: Claims	1-10
	No: Claims	

2. Citations and explanations

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2005/001883

Re Item III.

The specific sequences of claims 11, 23, 26, 29, 32, 35, 38, 41, 44, 47, 49, 52-77 have not, according to PCT Rule 13ter.1.c, not been searched since the Sequence Listing as present in the description does not comply with WIPO Standard ST25 prescribed in the administrative instructions under Rule 5.2. The Sequence Listing has been furnished neither in paper form nor in machine readable form as provided for in the same instructions and the applicant has not remedied the disclosed deficiencies within the time limit fixed in the invitation pursuant to PCT Rule 13ter.1.a.

As these claims have not been searched, they shall not be examined. Claims 12-22, 24, 25, 27, 28, 30, 31, 33, 34, 36, 37, 39, 40, 42, 43, 45, 46, 48, 50, 51 which incorporate the features of the above mentioned non-searched claims were only searched insofar as they did not relate to sequences.

Claims 13-22, 24, 25, 27, 28, 30, 31, 33, 34, 36, 37, 39, 40, 42, 43, 45, 46, 48, 50, 51 relate to subject matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject matter of these claims (Article 34(4)(a)(i) PCT)

Re Item IV.

The separate inventions are considered to be:

Invention 1

1-10, 12-22, 24, 25, 27, 30, 33, 34, 36, 39, 40, 42, 45, 50, 51 (partially)

Relating to compositions or methods of treating disease employing a modulator of LRP4 activity.

Invention 2

28, 37, 48 (completely), 1-10, 12-22, 24, 25, 27, 30, 31, 33, 36, 39, 42, 43, 45, 50, 51 (partially)

Relating to compositions or methods of treating disease employing a modulator of LRP8 activity.

Invention 3

46 (completely), 1-10, 12, 22, 24, 25, 27, 30, 31, 33, 34, 36, 39, 40, 42, 43, 45, 50, 51.

Relating to compositions or methods of treating disease employing a modulator of LRP2 (megalin) activity.

They are not so linked as to form a single general inventive concept (Rule 13.1 PCT) for the following reasons:

The problem sought to be solved by the present application is to provide pharmaceutical compositions for the treatment of disease

The applicant solves this problem by providing three solutions, namely antibodies which interfere with the activity of

1. LRP4
2. LRP8
3. LRP2

The common concept linking these separate inventions is that these three gene products are all involved in disease. This concept, however is not new as WO03095678 discloses that bone disease may be treated by administration of an antibody against LRP2. In view of the fact that no other technical features can be acknowledged which, in light of the prior art could be regarded as special technical features, the ISA is of the opinion that there is no single inventive concept underlying the plurality of claimed inventions of the present application in the sense of Rule 13.1 PCT.

However, given the nature of the subject matter, it was possible without undue extra burden to search all three inventions. All three inventions shall therefore be examined.

Re Item V.

For the assessment of the present claims 13-22, 24, 25, 27, 30, 33, 34, 36, 39, 40, 42, 45, 50, 51 on the question whether they are industrially applicable, no unified criteria exist within the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognise as industrially applicable the subject matter of claims to the use of a compound in medical treatment, but may allow, however, the use of such a compound for the manufacture of a medicament for a new medical treatment.

Cited Documents

Reference is made to the following documents:

D1 : WO 03/080103 A (MAX-DELBRUECK-CENTRUM FUER MOLEKULARE MEDIZIN;
WILLNOW, THOMAS) 2 October 2003 (2003-10-02)

D2 : WO 03/095678 A (CORNISH, JILLIAN,; REID, IAN, REGINALD,; PALMANO, KAY,
PATRICIA,; GREY) 20 November 2003 (2003-11-20)

Article 33(2) PCT

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-10, 12-14, 18, 22, 50, 51 is not new in the sense of Article 33(2) PCT.

The document D1 discloses the disruption of LRP2 (Megalin) activity as a result of the interaction of a drug with the megalin receptor. Drugs performing this task may be used in a variety of therapeutic settings (cf page 7, lines 14-25; page 20, lines 14-19; claims). As a consequence of this disclosure, the subject matter of claims 1-3,5,9,10,13,14,18,22, 50 and 51 is not novel (Article 33(2) PCT).

The document D2 discloses the use of antibody antagonists specific for LRP2 in the therapy of various ailments (cf page 2, line 13-25; page 4, lines 1-13; claims 27-44). The subject matter of claims 1, 3-10, 12, 14, 18, 50 and 51 is not new in light of this document)

The subject matter of claims 15-17, 19-21, 24, 25, 27, 28, 30, 31, 33, 34, 36, 37, 39, 40, 42, 43, 45, 46 and 48 is novel with regard to the prior art.

Article 33(3) PCT

For claim 15, the closest prior art is D2, which is described above.

The difference between claim 15 and D2 is that in claim 15, the disease to be treated is psoriasis.

The effect is that the treatment of psoriasis is attained in claim 15.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

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The problem to be solved is to provide a therapy for psoriasis.

The subject matter of claim 15 solves this problem but is not inventive as the applicant does not actually show that he has solved any problem since the application is devoid of any material showing that such a therapy might be feasible. As is this is the case for all of the therapeutic agents referred to in the claims (LRP2, LRP4 & LRP8), the same argumentation applies to the subject matter of claims 16,17, 19-21, 24, 25, 27, 28, 30, 31, 33, 34, 36, 37, 39, 40, 42, 43, 45, 46 and 48 which are not inventive for the same reasoning (Article 33(3) PCT).